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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,575	08/14/2001	Salih J. Wakil	D6374CIP	9113

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EXAMINER	
PARAS JR, PETER	
ART UNIT	PAPER NUMBER
1632	//

DATE MAILED: 07/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Applicati n No. 09/929,575	Applicant(s) WAKIL ET AL.	
	Examin r Peter Paras, Jr.	Art Unit 1632	

-- The MAILING DATE f this communicati n appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 24-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 August 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's preliminary amendment filed on 4/17/03 has been entered. Claims 1-14 and 16-23 have been cancelled. New claims 24-28 have been added. Claims 15 and 24-28 are pending and are under current consideration.

Election/Restrictions

Applicant's election without traverse of Group IV, claim 15, in Paper No. 10 is acknowledged.

Drawings

New corrected drawings are required in this application because the drawings submitted contain handwritten alterations. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

The instant abstract appears to comprise over 150 words.

Claim R j ctions - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15 and 24-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method to the extent a transgenic mouse whose genome comprises a homozygous disruption of an endogenous ACC2 gene for the acetyl-CoA carboxylase-2 isoform of acetyl-CoA carboxylase, wherein said disruption inactivates said gene and wherein said mouse does not produce any functional acetyl-CoA carboxylase-2 and exhibits a phenotype of comprising a metabolic reduction in malonyl-CoA production in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells, and consuming more calories than a wild type mouse yet accumulating less fat than a wild type mouse does not reasonably provide enablement for any other transgenic mice embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of screening for an inhibitor of acetyl-CoA carboxylase 2 isoform activity comprising administering to one or more wild type mouse and screening said one or more mouse for a phenotype exhibited by a transgenic mouse, wherein the phenotype is a metabolic reduction in malonyl-CoA production in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the

liver and fat storage cells, and consuming more calories than a wild type mouse yet accumulating less fat than a wild type mouse. The claims are further embrace a transgenic mouse comprising a mutation in an endogenous ACC2 gene.

The instant rejection is directed to the transgenic mouse embraced by the claims. The specification has taught a transgenic mouse, for use in the claimed method, whose genome comprises a homozygous disruption of the endogenous acetyl-CoA carboxylase-2 (ACC2) gene, wherein said disruption inactivates said gene, and wherein said mouse does not produce any functional ACC2. See pages 20-21. The specification has taught that the disruption entails inactivation of the exon that contains the biotin-binding motif Met-Lys-Met by homologous recombination with a heterologous nucleotide sequence. See page 19. The specification has also taught that such a mouse has phenotypes that comprise a metabolic reduction in malonyl-CoA in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells, and consumption of more calories than a wild type mouse yet accumulating less fat than a wild type mouse. See pages 21-31. The specification however has not taught other transgenic mice that exhibit such a phenotype. In addition, the specification has not taught a transgenic mouse comprising a heterozygous disruption of the endogenous ACC2 gene that has any discernible phenotype. The working examples and guidance provided by the instant specification fail to teach the skilled artisan how to use such mice, as they do not appear to have a phenotype. As such it would have required undue experimentation, given the lack of guidance provided

by the instant specification, for the skilled artisan to make and use the other transgenic mice encompassed by the claims without a reasonable expectation of success.

With regard to claim breadth, the standard under 112, first paragraph entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, in light of the specification, the claimed invention is properly interpreted with regard to the disclosed phenotype of the exemplified ACC2 (-/-) mice. **Such an interpretation is consistent with the specification despite that the claimed transgenic mice require only that they comprise a mutation that inactivates an endogenous ACC2 gene, wherein the mutation results in the lack of expression of functional ACC2.** This is because, with regard to the enablement requirement, one of skill in the art must be provided with both how to make and use the claimed invention. As such, the enabled scope of the claimed invention, in light of the teachings of the specification, is found to be the generation of transgenic ACC2 -/- mice which exhibit the phenotypes of lack of production of functional ACC2, a metabolic reduction in malonyl-CoA in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells, and consumption of more calories than a wild type mouse yet accumulating less fat than a wild type mouse.

Claim 15 embraces transgenic mice that exhibit a phenotype of a metabolic reduction in malonyl-CoA in skeletal muscle and heart, unrestricted fat oxidation and

reduced fat accumulation in the liver and fat storage cells, and consumption of more calories than a wild type mouse yet accumulating less fat than a wild type mouse. The specification however has taught that only a transgenic mouse whose genome comprises a homozygous disruption of an endogenous ACC2 gene for the acetyl-CoA carboxylase-2 isoform of acetyl-CoA carboxylase exhibits such a phenotype. The specification has not provided a correlation between disruption of other genes and a phenotype of a metabolic reduction in malonyl-CoA in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells, and consumption of more calories than a wild type mouse yet accumulating less fat than a wild type mouse in the context of a transgenic mouse. Absent evidence to the contrary, given the lack of guidance provided by the specification to that end, it would be unpredictable if disruption of other genes would result in such a phenotype. The state of the transgenic knockout art is such that disruption of a particular gene does not result in a predictable phenotype. See Moreadith et al. (Journal of Molecular Medicine, 1997) who support phenotypic unpredictability in knockout mice. In particular, Moreadith et al. discuss that gene targeting at a particular loci is unpredictable with respect to the resulting phenotype since often the generation of knockout mice, in many instances, changes the prevailing notions regarding the functions of the encoded proteins. For example, Moreadith et al. report that gene targeting at the endothelin loci led to the creation of mice with Hirschsprung's disease instead of the anticipated phenotype (abnormal control of blood pressure). See page 208, column 2, 2nd paragraph. See also Moens et al. (Development, 1993) who report the importance of generating

different mutations at a given locus to elucidate fully the function of a particular gene during development (page 485, Abstract). Given the lack of guidance provided by the instant specification it would have required undue experimentation to make and use the invention as claimed.

Claims 15 and 24-28 additionally can be interpreted to embrace transgenic mice comprising a heterozygous disruption of an endogenous ACC2 gene for the acetyl-CoA carboxylase-2 isoform of acetyl-CoA carboxylase that have a phenotype of a phenotype of a metabolic reduction in malonyl-CoA in skeletal muscle and heart, unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells, and consumption of more calories than a wild type mouse yet accumulating less fat than a wild type mouse. The specification however has only provided guidance that correlates such a phenotype with a homozygous disruption of the endogenous ACC2 gene for the acetyl-CoA carboxylase-2 isoform of acetyl-CoA carboxylase. Accordingly, the claims as written are not enabled because the embraced heterozygous transgenic mice do not exhibit the required phenotype. Given the lack of guidance provided by the instant specification with regard to a phenotype exhibited by heterozygous transgenic mice embraced by the claims it would have required undue experimentation to practice the invention as claimed.

Additionally, the claims as written do not require germline transmission of the ACC2 disruption and do not require that the disruption is present in the genome of the transgenic mouse. These two points are important because the claims as written embrace methods of *in vivo* and/or *in utero* gene transfer. Such methods are

unpredictable in the art and are not supported or enabled by the instant specification. The Examiner acknowledges that the instant specification does not contemplate such methods but the as the claims however do embrace such methods, appropriate amendments to the claims are necessary to place the instant application in condition for allowance.

Accordingly, in view of the quantity of experimentation necessary for the production and use of transgenic mice in the claimed methods, it would have required undue experimentation for one skilled in the art to make and/or use the transgenic mice embraced by the claims.

Note: An amendment to the claims with regard to the embraced transgenic mice as follows may be sufficient to overcome the instant rejection: A transgenic mouse whose genome comprises a homozygous disruption of an endogenous ACC2 gene for the acetyl-CoA carboxylase-2 isoform of acetyl-CoA carboxylase, wherein said disruption inactivates said gene and wherein said mouse does not produce any functional acetyl-CoA carboxylase-2.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is incomplete as written. The preamble of the claim is directed to a method of screening for an inhibitor of acetyl-CoA carboxylase 2 isoform activity. The claim however is incomplete because the steps of the method do not set forth the goal of the preamble in a positive process. Appropriate correction is required. Claims 24-28 depend form claim 15.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

PETER PARAS
PATENT EXAMINER

Art Unit 1632

Pete Paras